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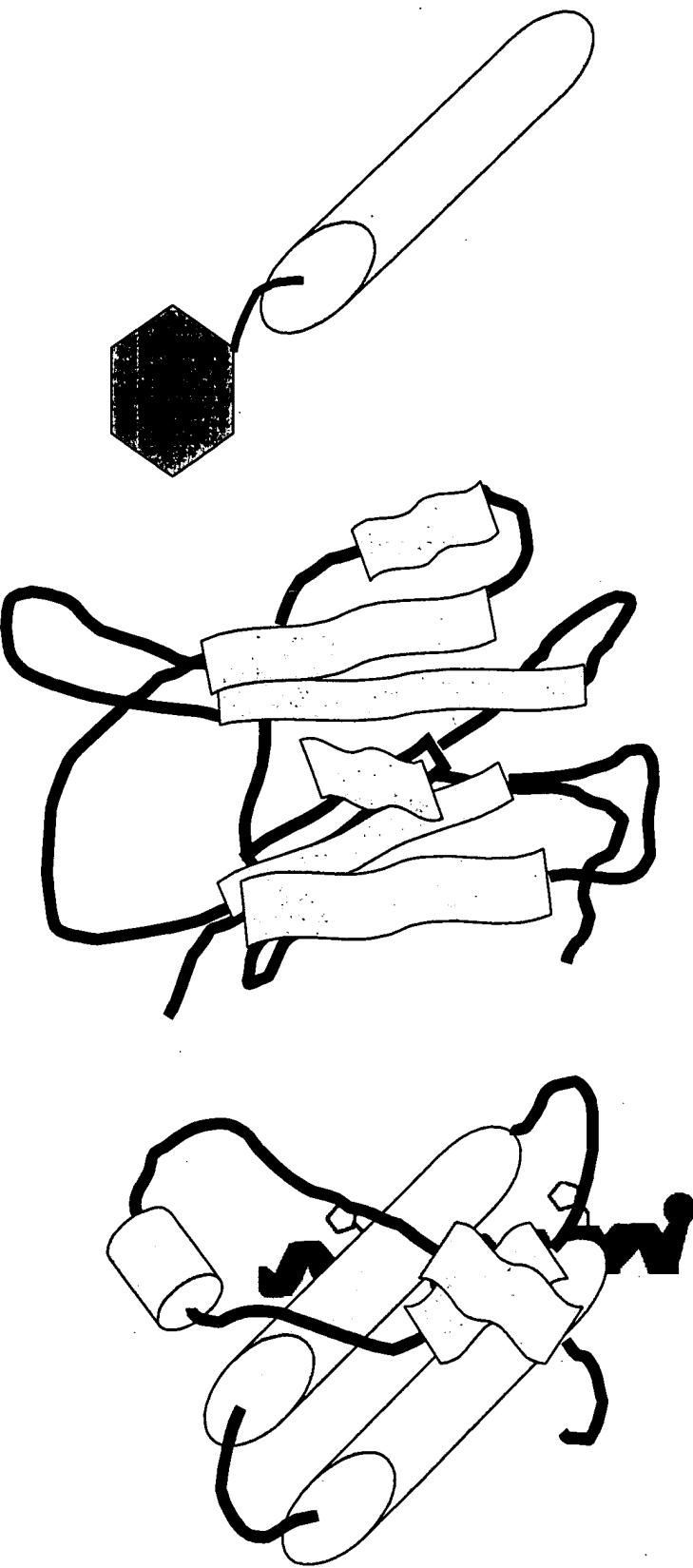
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**Transmissible spongiform encephalopathies:  
TSE Conformers**



**Labeled peptide fragment**  
**β-sheet Toxic form**  
**α-helix Non-toxic form**

Figure 1

## TSE Detection Schema

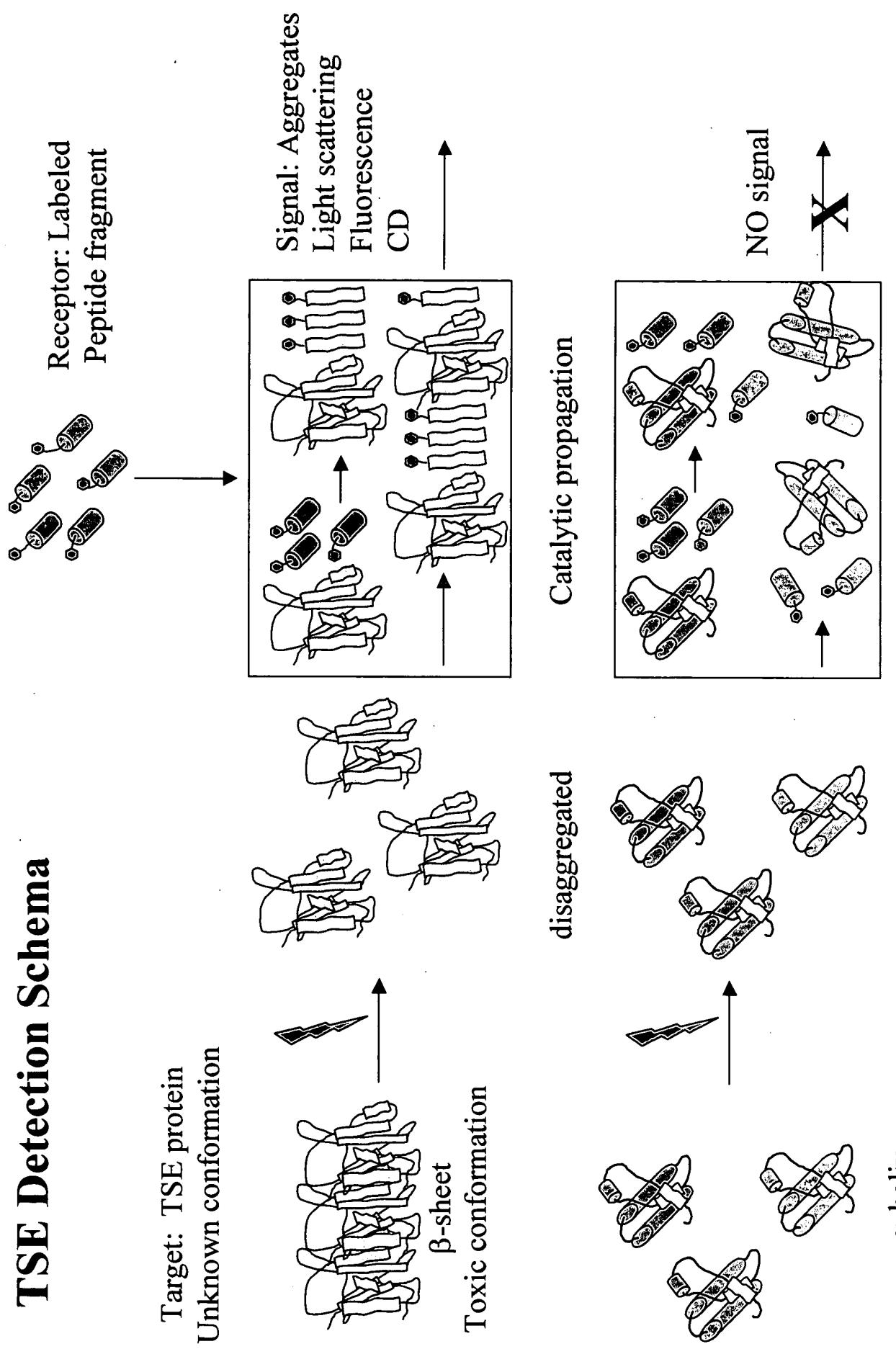


Figure 2

Non-toxic conformation

## Circular Dichroism Indicating Conformational Change

Poly-L-Lysine 20  $\mu\text{M}$  52,000 MW

Initial test peptide system

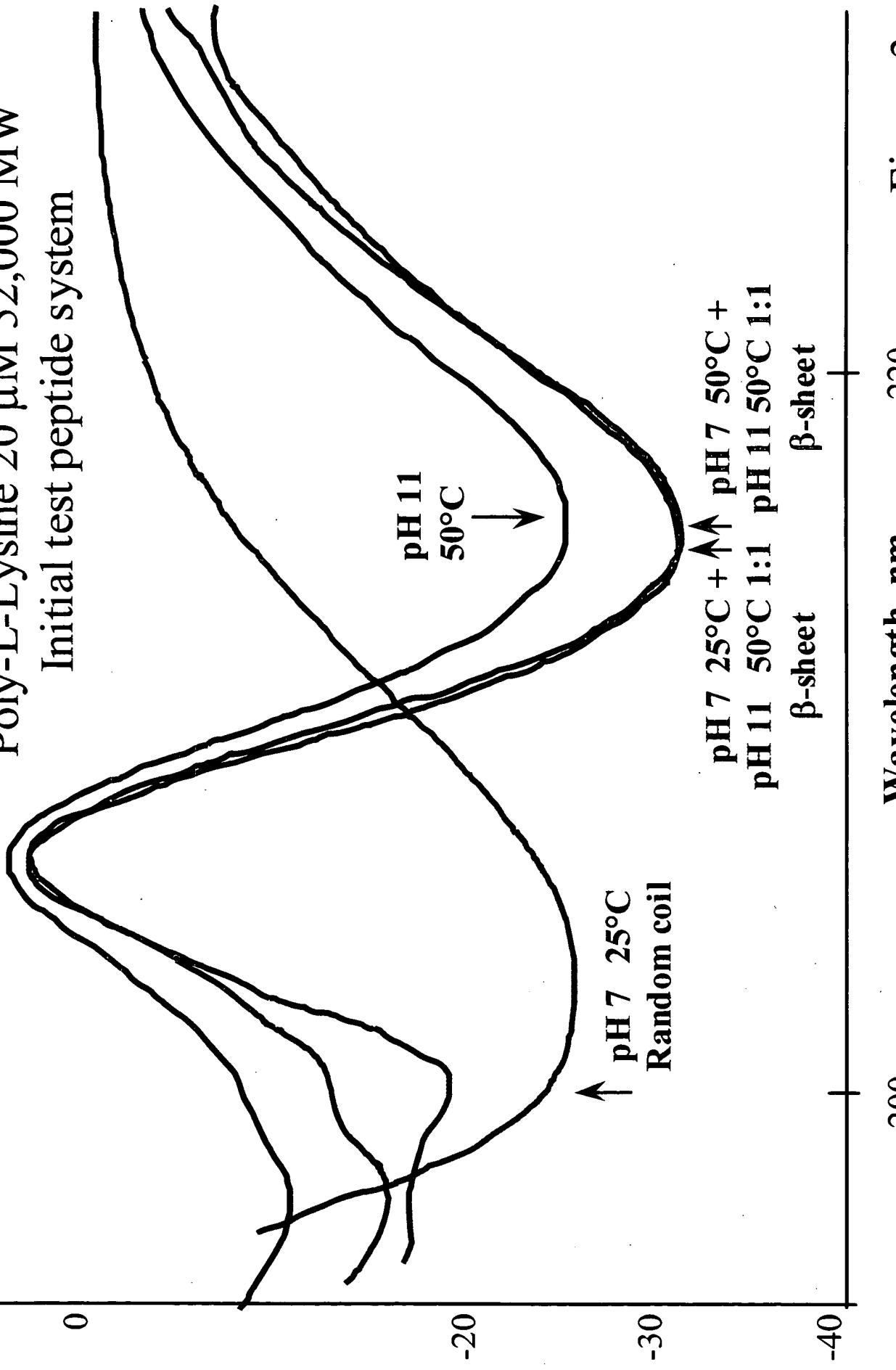
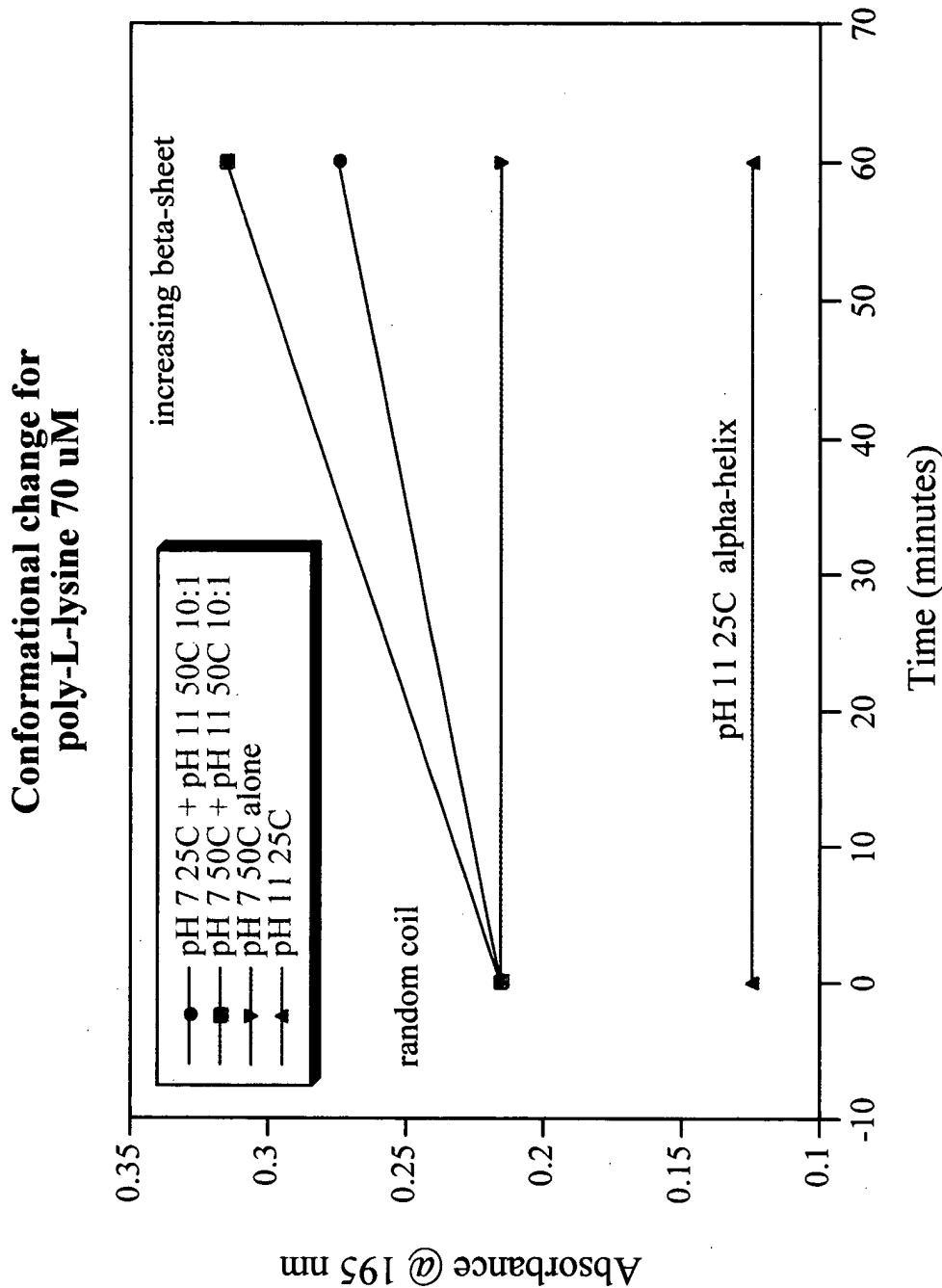


Figure 3

**Figure 4**



# Circular Dicroism (CD) of Poly-L-Lysine varying Temp and pH

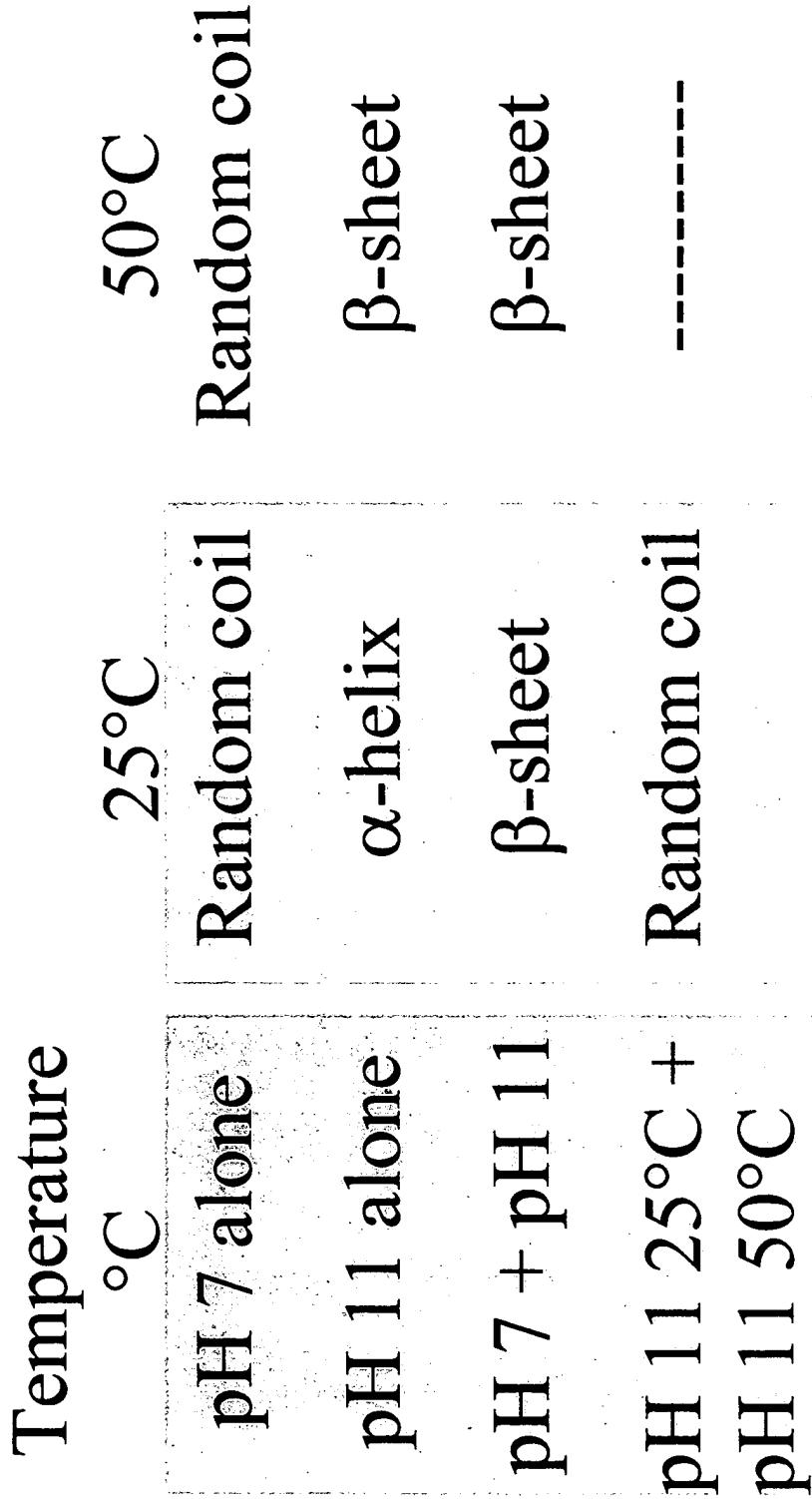
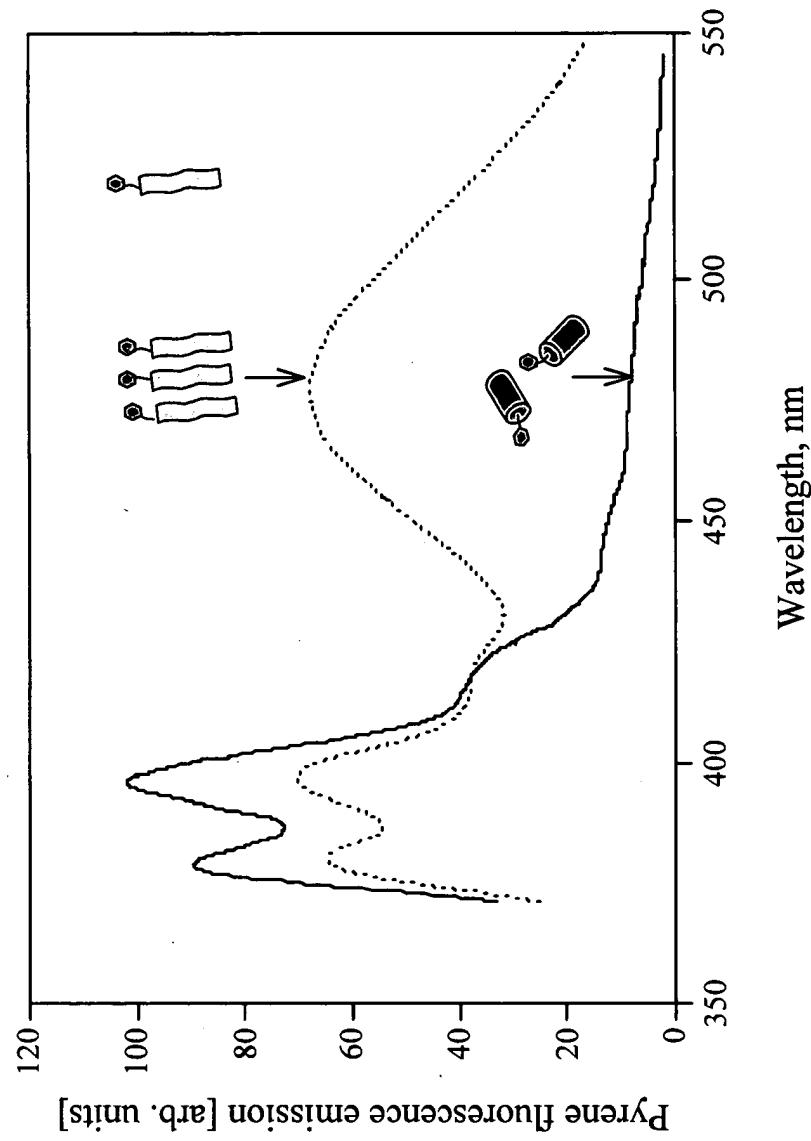


Figure 5

## Experiments with fluorescent probes for detection.

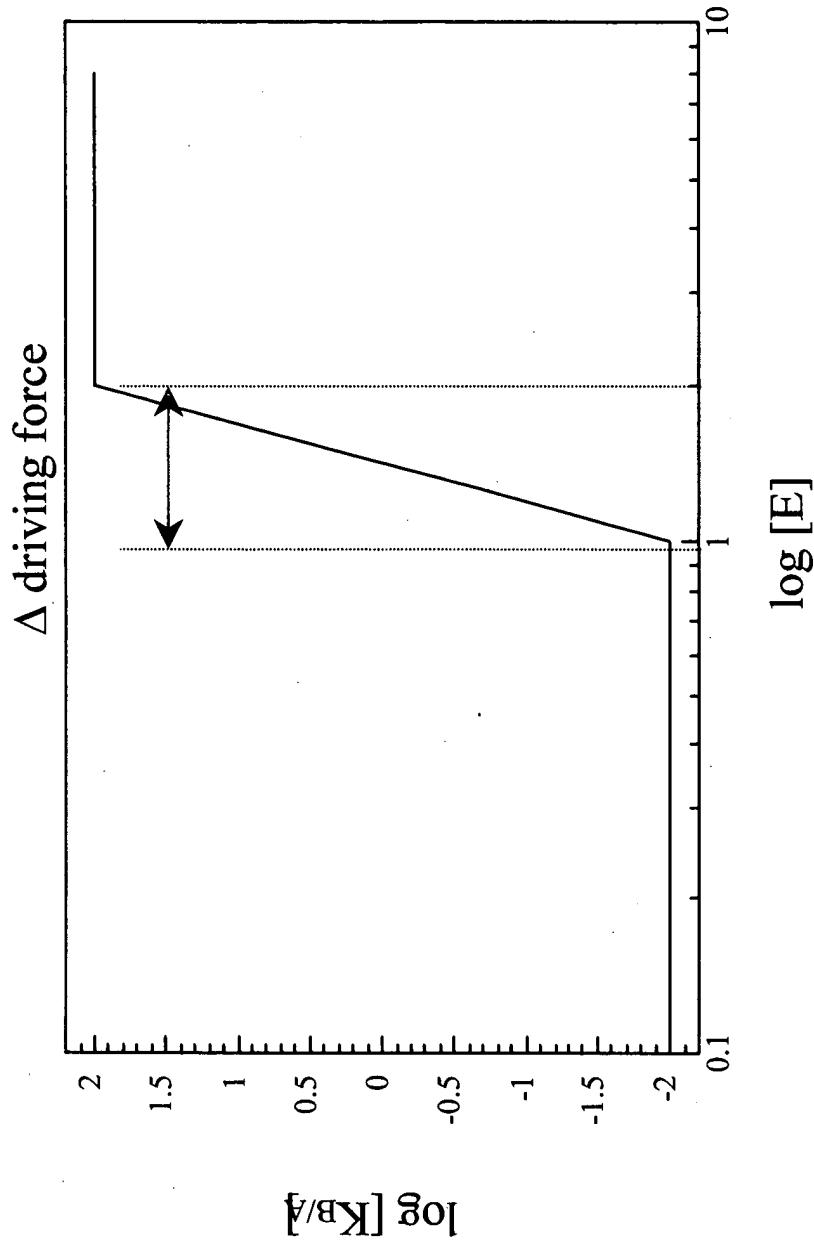
The data are from previous FRET experiments for proximal and distal locations in an  $\alpha$ -helical bundle structure undergoing conformational change.



The spectra shown are for pyrene excimer formation at 480 nm, but other probes (FITC, etc.) can be used.

Figure 6

# Engineering considerations for sensor design

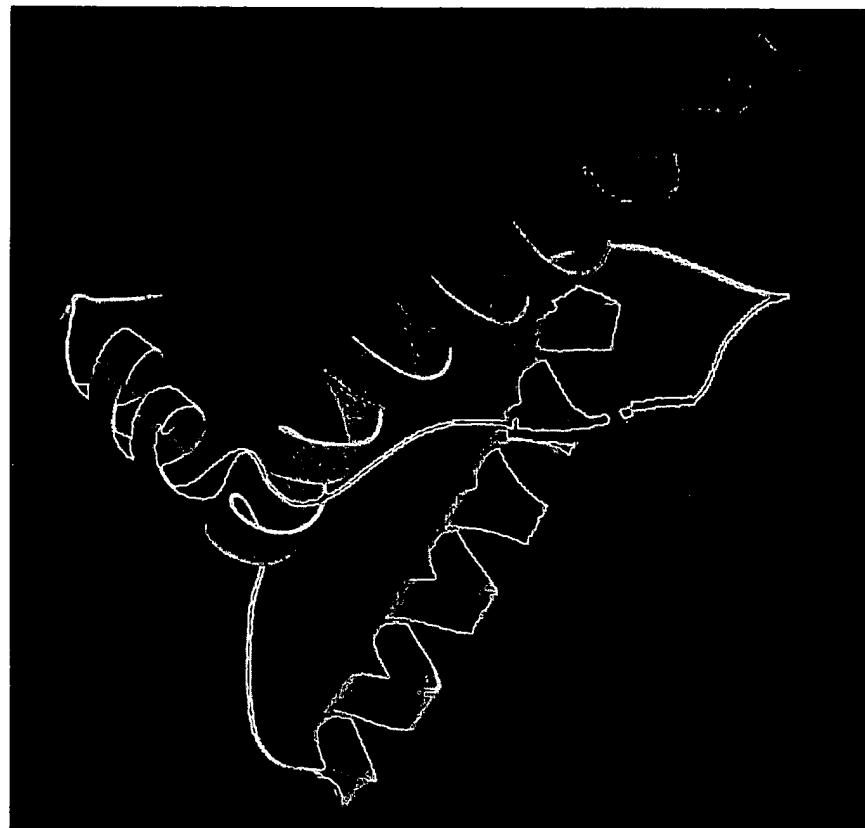


The **driving force** must be commensurate with the **energetic difference** between the two conformational states

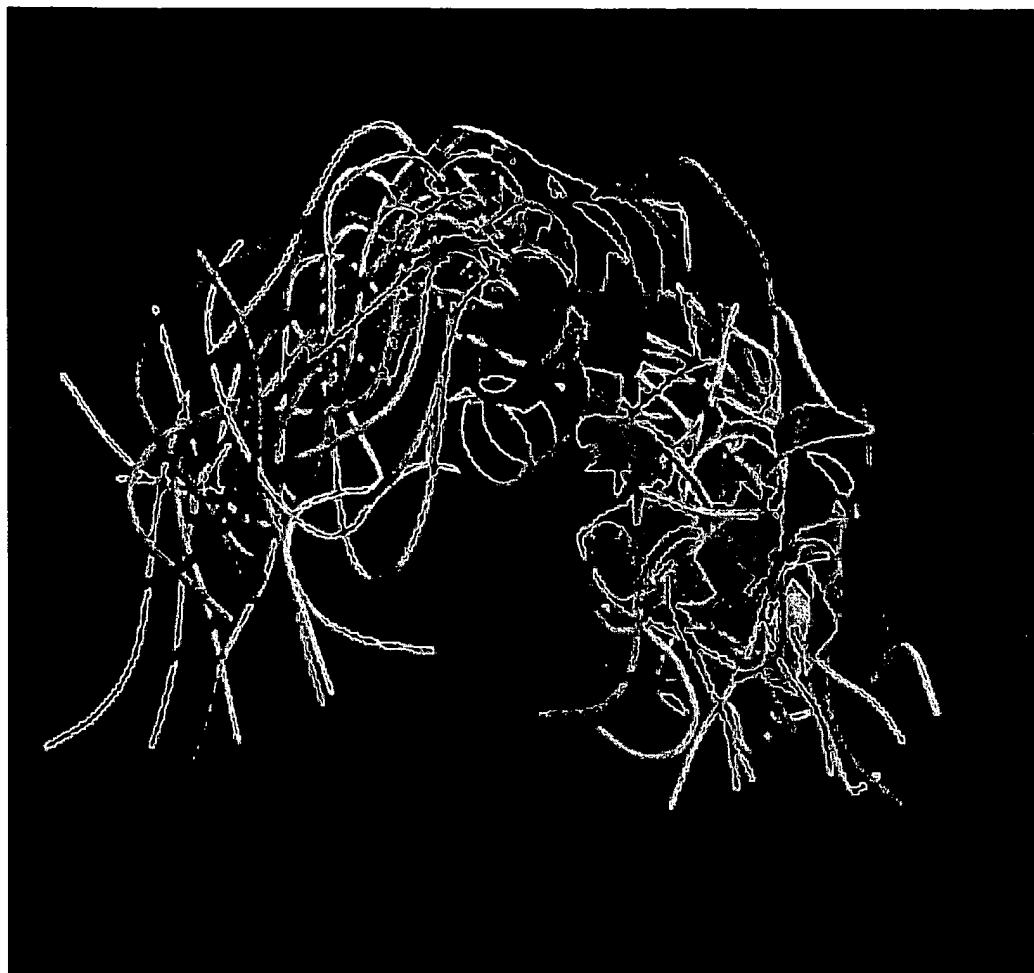
The process is driven by a **differential interaction** of the target peptide E, with the two conformations of the test PrP molecule.

Figure 7

**Figure 8**



**Figure 9**



## FIGURE 10

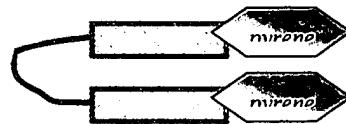
A.  
33mer palindrome  
VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV

19\_mer      KPKTNILKHVAGAAAAGAVV

14\_mer      LKHVAGAAAAGAVV

B.

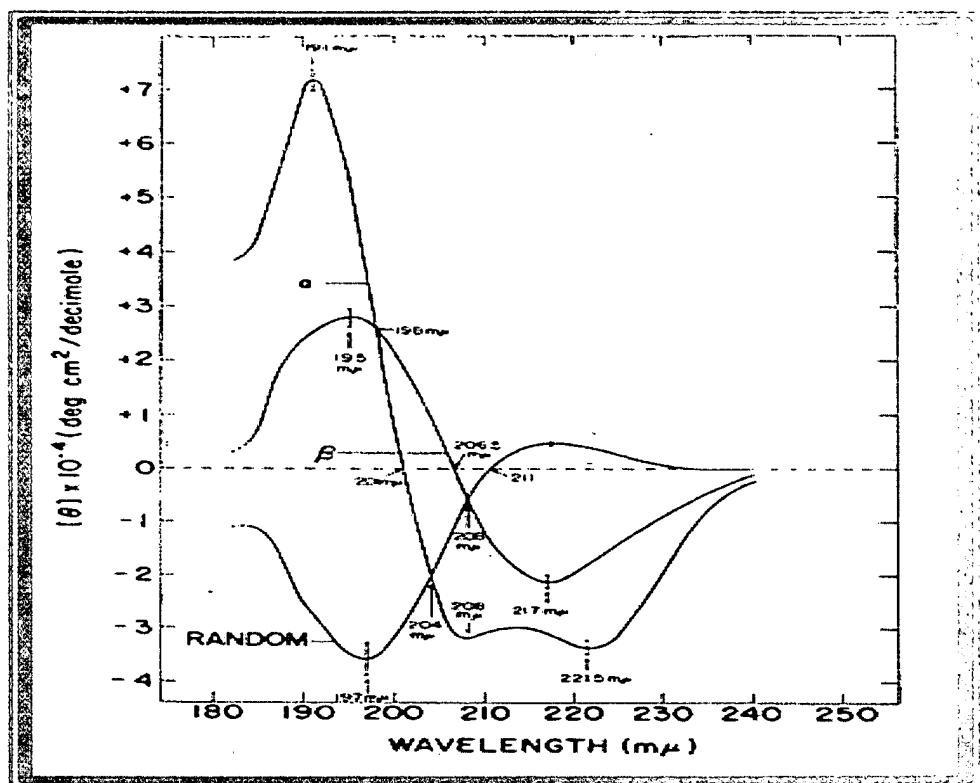
TNLKHVAGAAAAGAVV  
K  
PKLKHVAGAAAAGAVV



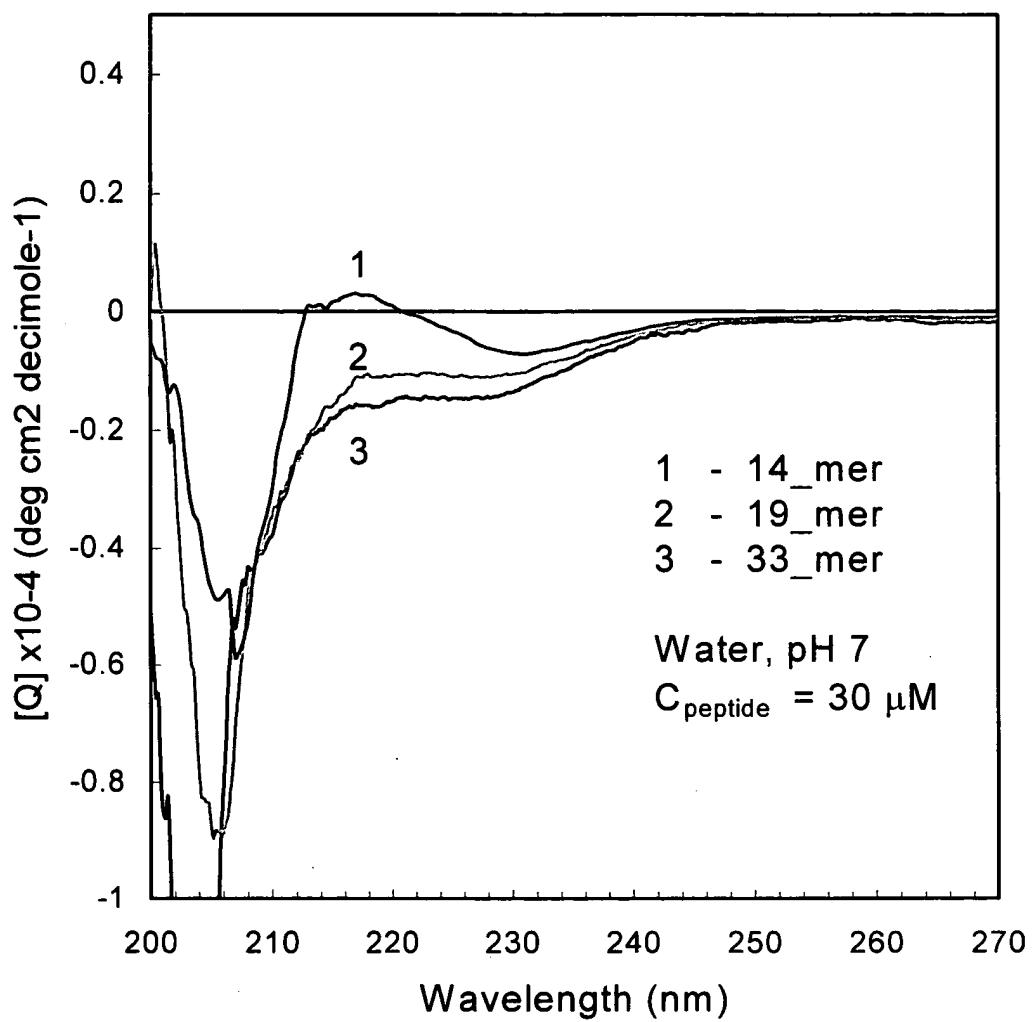
**Figure 10. Palindromic 33mer peptide probe.**

- A. Linear sequence of 33mer, 19mer and 14mer with palindromic sequences underlined and murine substituted V's and L's replace human/hamster sequence M's
- B. Folded sequence demonstrating parallel palindrome and diagram showing pyrene molecules present on both ends of the peptide forming an excimer structure.

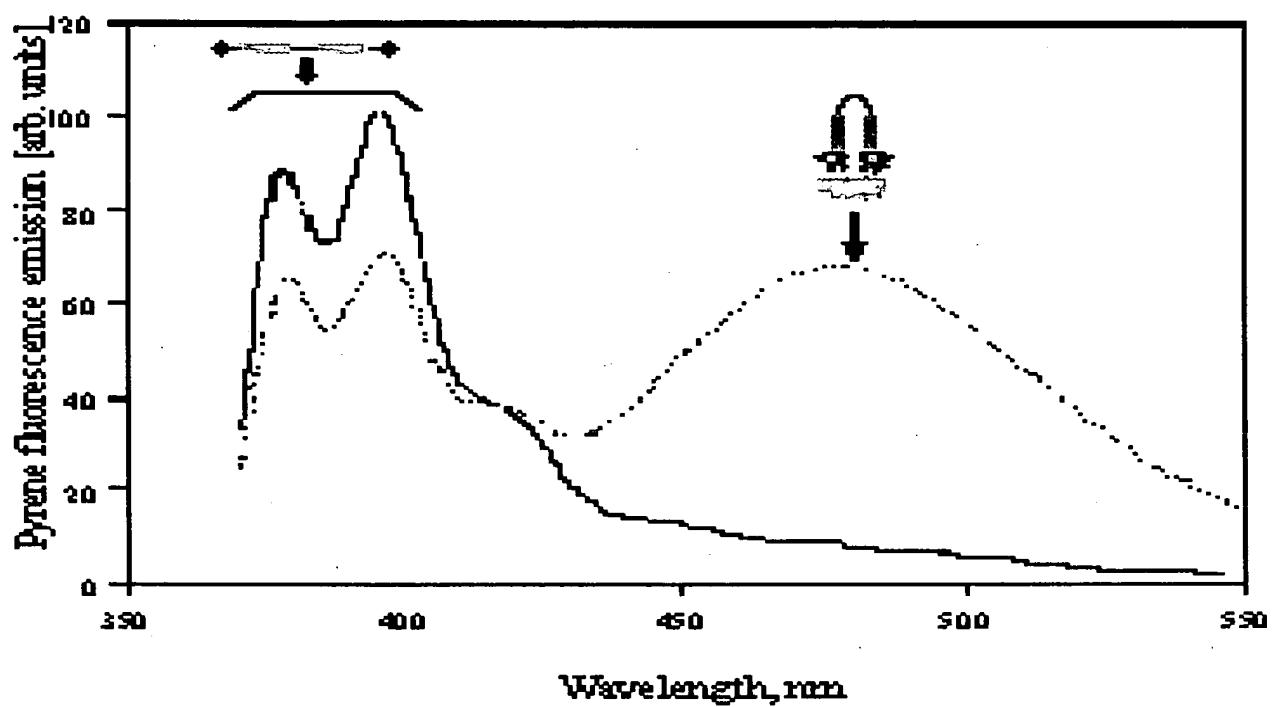
**FIGURE 11**



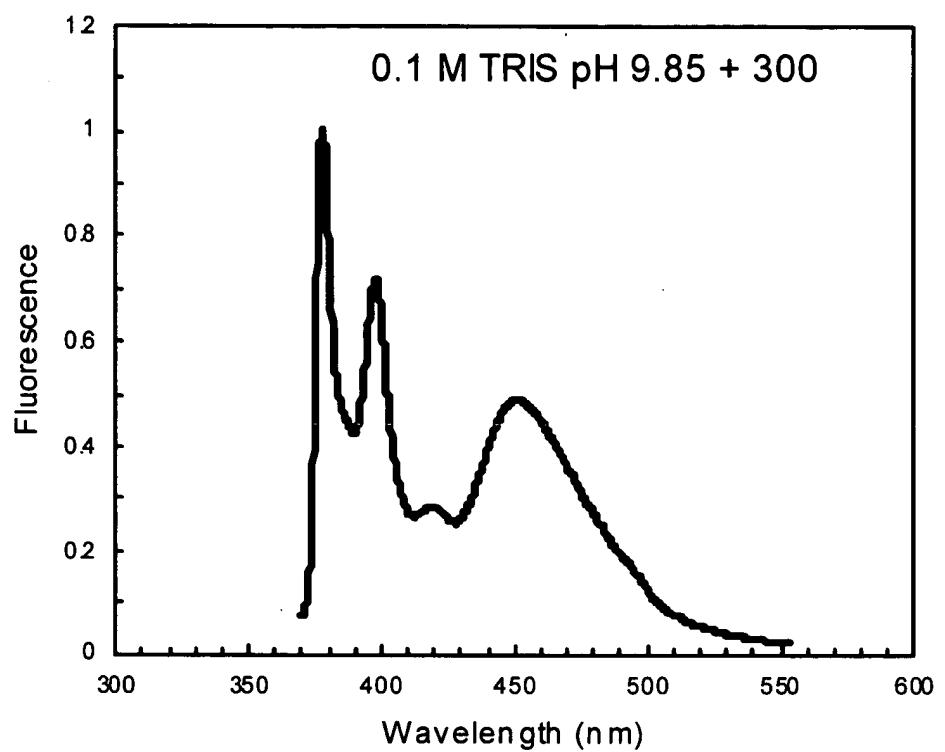
**FIGURE 12**



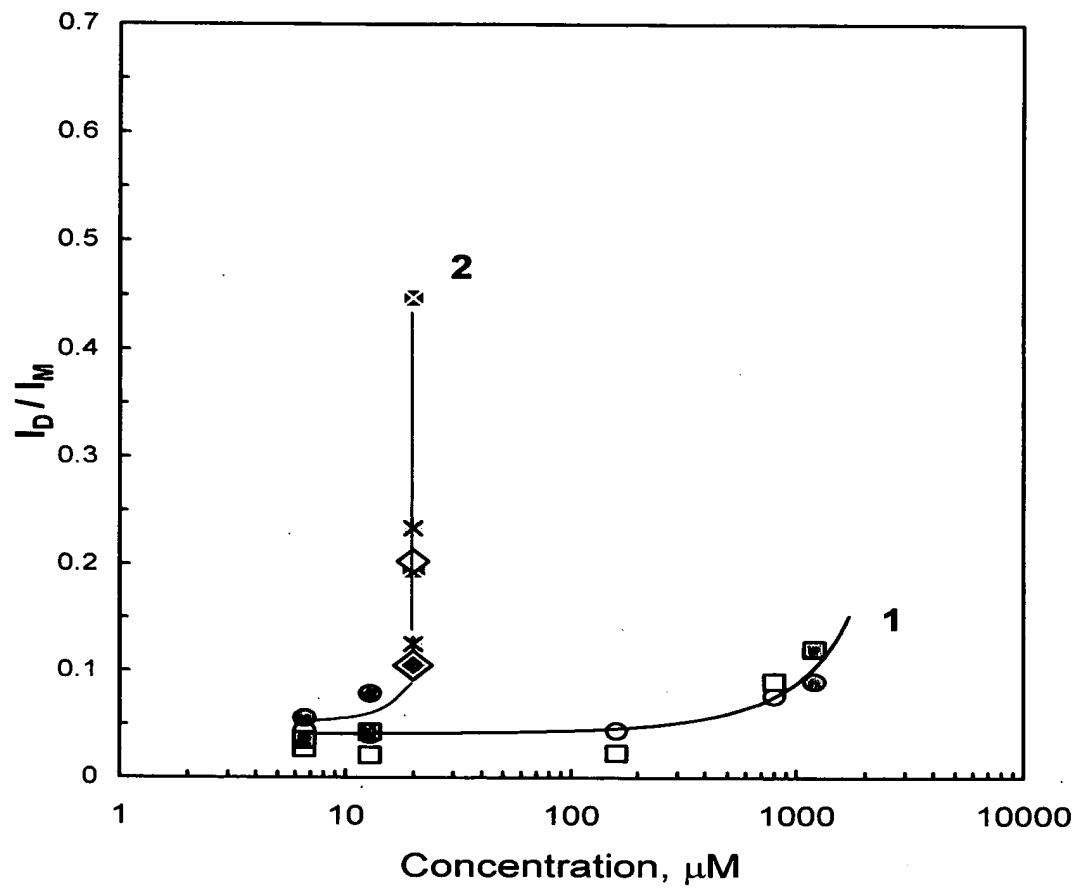
**FIGURE 13**



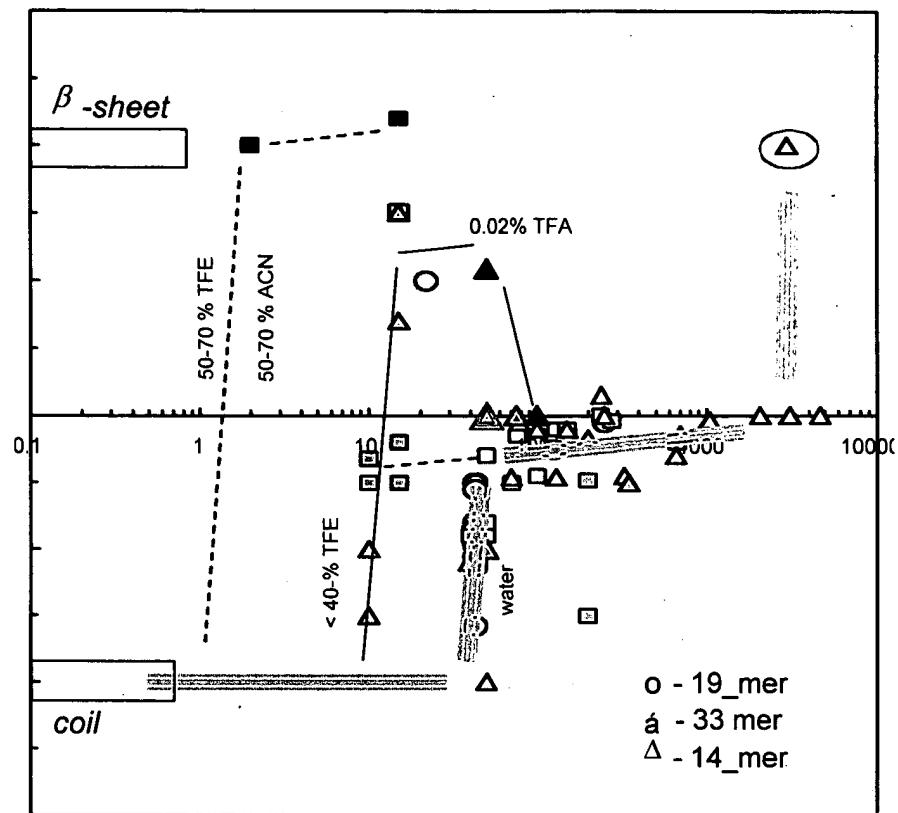
**FIGURE 14**



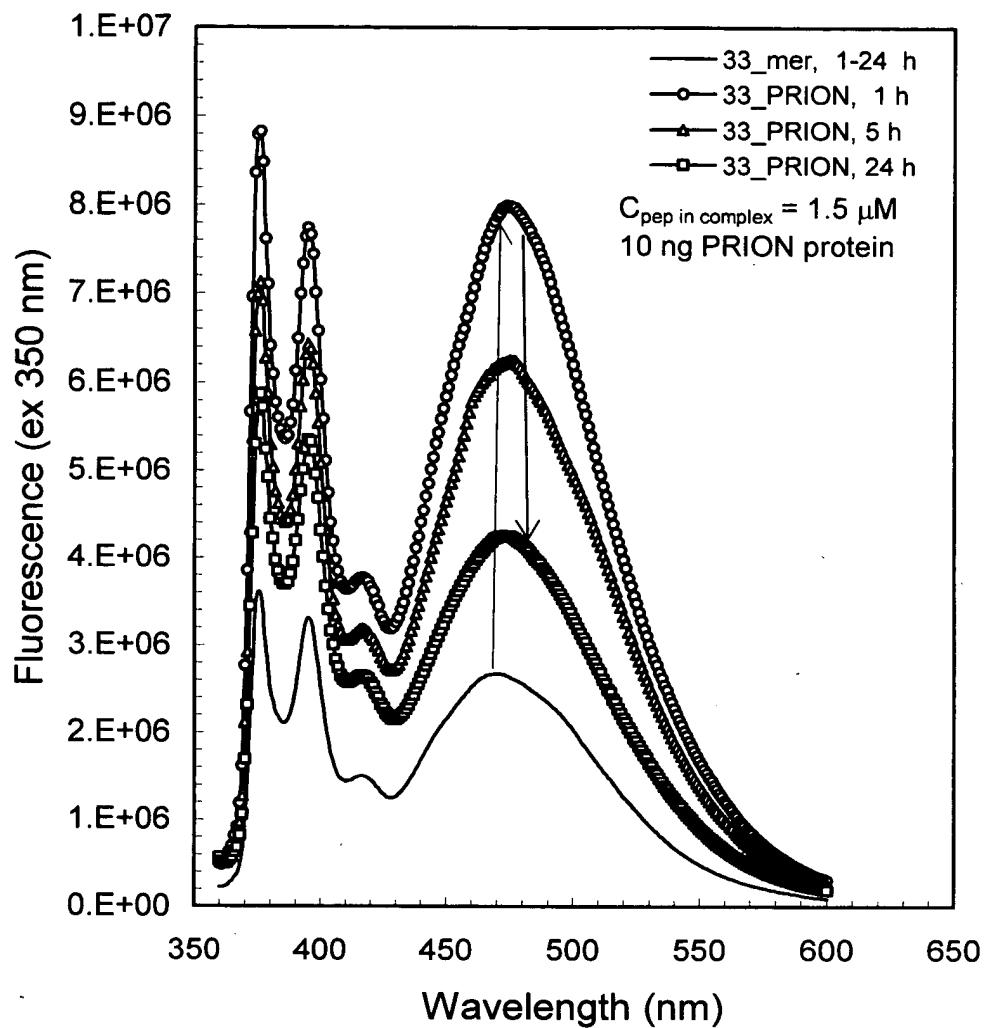
**FIGURE 15**



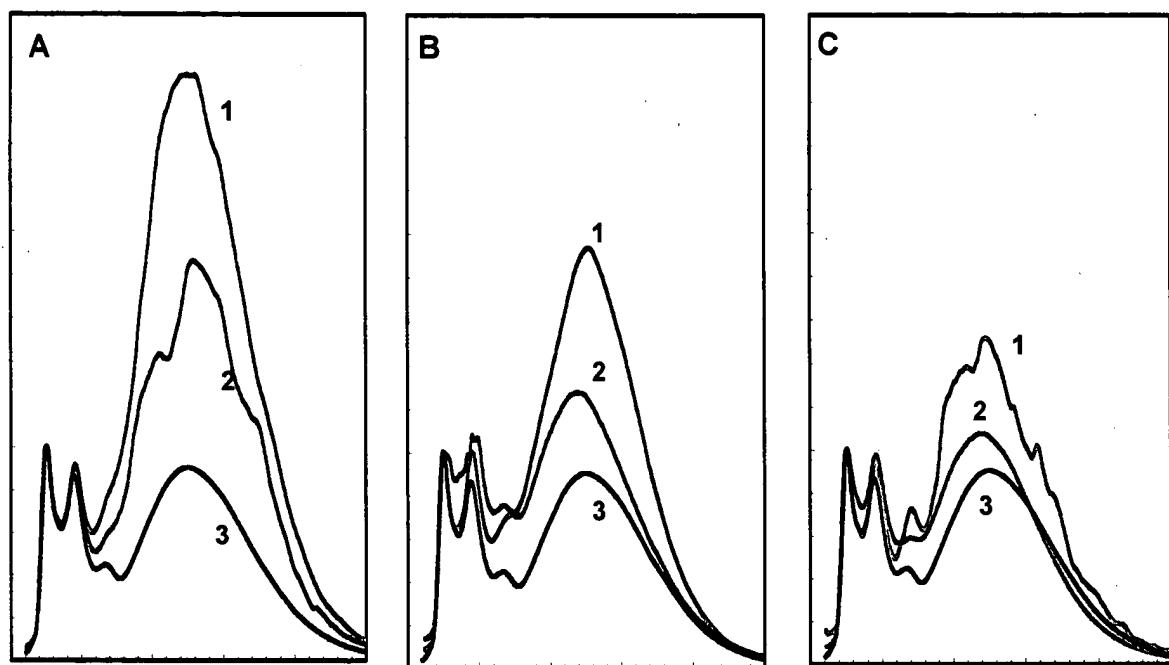
**FIGURE 16**



**FIGURE 17**



**FIGURE 18**



**FIGURE 19**

